



Clinical trial results:

Open-label, multicenter, single arm, phase II study assessing treatment patient preference for new deferasirox formulation (film-coated tablet) compared to the reference deferasirox dispersible tablet formulation

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-002282-61 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 11 March 2021 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 22 September 2021 |
| First version publication date | 22 September 2021 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CICL670FIC05 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02993224 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com |

Notes:

Paediatric regulatory details

| | |
|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 11 March 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 11 March 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective was to evaluate patient preference between deferasirox film-coated tablets (FCTs) and deferasirox dispersible tablets (DTs)

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 27 July 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Turkey: 10 |
| Country: Number of subjects enrolled | Egypt: 45 |
| Country: Number of subjects enrolled | Lebanon: 5 |
| Country: Number of subjects enrolled | Saudi Arabia: 17 |
| Country: Number of subjects enrolled | Morocco: 8 |
| Country: Number of subjects enrolled | Thailand: 51 |
| Country: Number of subjects enrolled | Vietnam: 12 |
| Worldwide total number of subjects | 148 |
| EEA total number of subjects | 0 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |

| | |
|---------------------------|----|
| Children (2-11 years) | 73 |
| Adolescents (12-17 years) | 20 |
| Adults (18-64 years) | 54 |
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants took part in 17 investigative sites in 7 countries

Period 1

| | |
|------------------------------|-----------------------|
| Period 1 title | Core Phase - Period 1 |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|--|
| Arm title | Deferasirox DT followed by deferasirox FCT |
|------------------|--|

Arm description:

Participants were treated with deferasirox DT followed by deferasirox FCT (core phase). Those who entered the extension phase were treated with deferasirox FCT

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Deferasirox |
| Investigational medicinal product code | ICL670 |
| Other name | |
| Pharmaceutical forms | Dispersible tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Deferasirox DT was provided as 125 mg, 250 mg, 500 mg dispersible tablets for oral use. The strengths provided in an individual country could differ and reflected the strengths available commercially in each country.

For iron chelation naive participants, the starting dose on Baseline Day 1 was 20 mg/kg/day in TDT and 10 mg/kg/day in NTDT.

For iron chelation (deferioxamine and/or deferiprone) participants, the starting dose was equivalent to the dose of deferioxamine received (for participants pre-treated with deferioxamine) and based on their serum ferritin levels (for participants pre-treated with deferiprone).

Participants took deferasirox DT once daily for 24 weeks (core phase). The required number of deferasirox DT tablets were to be dispersed with gentle stirring in a glass of water.

| Number of subjects in period 1 | Deferasirox DT followed by deferasirox FCT |
|---------------------------------------|--|
| Started | 148 |
| Completed | 140 |
| Not completed | 8 |
| Consent withdrawn by subject | 1 |
| Adverse event, non-fatal | 4 |
| Lost to follow-up | 3 |

Period 2

| | |
|------------------------------|----------------------|
| Period 2 title | Core Phase- Period 2 |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|--|
| Arm title | Deferasirox DT followed by deferasirox FCT |
|------------------|--|

Arm description:

Participants were treated with deferasirox DT followed by deferasirox FCT (core phase). Those who entered the extension phase were treated with deferasirox FCT

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Deferasirox |
| Investigational medicinal product code | ICL670 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Deferasirox FCT was provided as 90 mg, 180 mg, 360 mg film coated tablets for oral use. The FCT starting dose on Week 25 was 14 mg/kg/day in TDT and 7 mg/kg/day in NTDT.

Participants took deferasirox FCT once daily for 24 weeks during the core phase. For patients with difficulties in swallowing deferasirox FCT, it was allowed to crush the film-coated tablets and administer the study drug by sprinkling the full dose on soft food (like yogurt or apple puree).

| Number of subjects in period 2 | Deferasirox DT followed by deferasirox FCT |
|--|--|
| Started | 140 |
| Completed | 136 |
| Not completed | 4 |
| Adverse event, non-fatal | 1 |
| Unwillingness To Comply With Protocol Procedures | 2 |
| Allogenic stem cell transplantation | 1 |

Period 3

| | |
|------------------------------|-----------------|
| Period 3 title | Extension Phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|---|--|
| Arm title | Deferasirox DT followed by deferasirox FCT |
| Arm description: Participants were treated with deferasirox DT followed by deferasirox FCT (core phase). Those who entered the extension phase were treated with deferasirox FCT | |
| Arm type | Experimental |
| Investigational medicinal product name | Deferasirox |
| Investigational medicinal product code | ICL670 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Deferasirox FCT was provided as 90 mg, 180 mg, 360 mg film coated tablets for oral use. Participants took deferasirox FCT once daily up to 48 weeks during the extension phase. For patients with difficulties in swallowing deferasirox FCT, it was allowed to crush the film-coated tablets and administer the study drug by sprinkling the full dose on soft food (like yogurt or apple puree).

| Number of subjects in period 3^[1] | Deferasirox DT followed by deferasirox FCT |
|---|--|
| Started | 116 |
| Completed | 80 |
| Not completed | 36 |
| Consent withdrawn by subject | 3 |
| Adverse event, non-fatal | 3 |
| Unwillingness To Comply With Protocol Procedures | 1 |
| Deferasirox FCT locally reimbursed | 27 |
| Lost to follow-up | 2 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who completed the core phase started the extension phase (optional)

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Deferasirox DT followed by deferasirox FCT |
|-----------------------|--|

Reporting group description:

Participants were treated with deferasirox DT followed by deferasirox FCT (core phase). Those who entered the extension phase were treated with deferasirox FCT

| Reporting group values | Deferasirox DT followed by deferasirox FCT | Total | |
|--|--|-------|--|
| Number of subjects | 148 | 148 | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 73 | 73 | |
| Adolescents (12-17 years) | 20 | 20 | |
| Adults (18-64 years) | 54 | 54 | |
| From 65-84 years | 1 | 1 | |
| 85 years and over | 0 | 0 | |
| Age Continuous Units: Years | | | |
| arithmetic mean | 15.32 | | |
| standard deviation | ± 13.824 | - | |
| Sex: Female, Male Units: Participants | | | |
| Female | 82 | 82 | |
| Male | 66 | 66 | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Indian (Indian subcontinent) | 5 | 5 | |
| Other | 143 | 143 | |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Deferasirox DT followed by deferiasirox FCT |
| Reporting group description: Participants were treated with deferiasirox DT followed by deferiasirox FCT (core phase). Those who entered the extension phase were treated with deferiasirox FCT | |
| Reporting group title | Deferasirox DT followed by deferiasirox FCT |
| Reporting group description: Participants were treated with deferiasirox DT followed by deferiasirox FCT (core phase). Those who entered the extension phase were treated with deferiasirox FCT | |
| Reporting group title | Deferasirox DT followed by deferiasirox FCT |
| Reporting group description: Participants were treated with deferiasirox DT followed by deferiasirox FCT (core phase). Those who entered the extension phase were treated with deferiasirox FCT | |
| Subject analysis set title | Deferasirox DT followed by deferiasirox FCT (Full Analysis Set) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants to whom study treatment was assigned and who received at least one dose of each study treatment (deferiasirox DT and FCT). | |

Primary: Number of participants preferring deferiasirox FCT or DT at Week 48 based on preference questionnaire (item 2)

| | |
|---|---|
| End point title | Number of participants preferring deferiasirox FCT or DT at Week 48 based on preference questionnaire (item 2) ^[1] |
| End point description: Number of participants preferring deferiasirox FCT or DT as measured by preference questionnaire (item 2) at Week 48. The preference questionnaire was a 3-item questionnaire. At Week 48, the second item of the preference questionnaire asked the patients (or parents of young patients from 2 to 9 years old) which medicine did the patient "like best": "Tablet to dissolve in liquid" (=deferiasirox DT), "Film coated tablet" (=deferiasirox FCT), "Sprinkle powder on food" (=deferiasirox FCT) and "I don't know" (=none of the above). The number of participants who selected each response option for item 2 was assessed. The analysis was performed for participants who answered the item 2 of the preference questionnaire. | |
| End point type | Primary |
| End point timeframe: Week 48 | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to EudraCT system limitations, no statistical analyses have been specified for the endpoints, as this is a single arm study and comparisons within an arm are not supported by the system

| | | | | |
|----------------------------------|---|--|--|--|
| End point values | Deferasirox DT followed by deferiasirox FCT (Full Analysis Set) | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 134 | | | |
| Units: Participants | | | | |
| Preference for deferiasirox DT | 10 | | | |
| Preference for deferiasirox FCT | 121 | | | |
| Preference for none of the above | 3 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants preferring deferasirox FCT, deferasirox DT or previous iron chelation therapy at Week 28 based on preference questionnaire (item 2)

| | |
|-----------------|--|
| End point title | Number of participants preferring deferasirox FCT, deferasirox DT or previous iron chelation therapy at Week 28 based on preference questionnaire (item 2) |
|-----------------|--|

End point description:

Number of participants preferring deferasirox FCT, deferasirox DT or previous iron chelation therapy as measured by preference questionnaire (item 2) at Week 28. The preference questionnaire was a 3-item questionnaire. At Week 28, the second item of this questionnaire asked the patients (or parents of young patients from 2 to 9 years old) which medicine did the patient "like best": "Tablet to dissolve in liquid" (=deferasirox DT), "Film coated tablet (taken once a day)" (=deferasirox FCT), "Sprinkle powder on food" (=deferasirox FCT), "Tablet (taken 3 times a day)" (=previous iron chelation therapy), "Injection" (=previous iron chelation therapy) and "I don't know" (=none of the above). The number of participants who selected each response option for item 2 was assessed. This analysis was performed only for patients who had received iron chelation therapy prior to enrolling in the study and who answered the item 2 of the preference questionnaire.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 28

| | | | | |
|---------------------------------------|--|--|--|--|
| End point values | Deferasirox DT followed by deferasirox FCT (Full Analysis Set) | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 69 | | | |
| Units: Participants | | | | |
| Preference for deferasirox DT | 6 | | | |
| Preference for deferasirox FCT | 60 | | | |
| Preference for iron chelation therapy | 3 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants preferring deferasirox DT or previous iron chelation therapy at Week 4 and Week 24 based on preference questionnaire (item 2)

| | |
|-----------------|--|
| End point title | Number of participants preferring deferasirox DT or previous |
|-----------------|--|

End point description:

Number of participants preferring deferasirox DT or previous iron chelation therapy as measured by preference questionnaire (item 2) at Week 4 and 24. The preference questionnaire was a 3-item questionnaire. At Week 4 and 24, the second item of the preference questionnaire asked the patients (or parents of young patients from 2 to 9 years old) which medicine did the patient "like best": "Tablet to dissolve in liquid" (=deferasirox DT), "Tablet (taken 3 times a day)" (=previous iron chelation therapy), "Injection" (=previous iron chelation therapy) and "I don't know" (=none of the above). The number of participants who selected each response option for item 2 was assessed. This analysis was performed only for patients who had received iron chelation therapy prior to enrolling in the study and who answered item 2 of the preference questionnaire

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|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 4 and Week 24

| End point values | Deferasirox DT followed by deferasirox FCT (Full Analysis Set) | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 70 | | | |
| Units: Participants | | | | |
| Preference for deferasirox DT (Week 4) | 57 | | | |
| Preference for iron chelation therapy (Week 4) | 11 | | | |
| Preference for none of the above (Week 4) | 2 | | | |
| Preference for deferasirox DT (Week 24) | 52 | | | |
| Preference for iron chelation therapy (Week 24) | 11 | | | |
| Preference for none of the above (Week 24) | 6 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants selecting each reason for treatment preference as assessed by the preference questionnaire at Week 28 and Week 48

| | |
|-----------------|--|
| End point title | Number of participants selecting each reason for treatment preference as assessed by the preference questionnaire at Week 28 and Week 48 |
|-----------------|--|

End point description:

The preference questionnaire was a 3 item questionnaire. The first item asked the patients (or parents of young patients from 2 to 9 years old) which medicine they were taking. The second item asked which of the medicines did the patient "Like best". Finally, the third item asked the patient why he/she preferred the medicine they chose in the second item. The number of participants who selected each response option for item 3 was assessed. Participants could select multiple reasons for treatment preference at each timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:
Week 28 and Week 48

| End point values | Deferasirox DT followed by deferasirox FCT (Full Analysis Set) | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 139 | | | |
| Units: Participants | | | | |
| Aftertaste (Week 28) | 9 | | | |
| Can correctly prepare the medicine (Week 28) | 35 | | | |
| Convenience (Week 28) | 109 | | | |
| Easier to remember to take the medicine (Week 28) | 57 | | | |
| Gain personal time with family/friends (Week 28) | 35 | | | |
| No/ less pain on the injection site (Week 28) | 31 | | | |
| No/ less side effects (Week 28) | 50 | | | |
| Number of pills (Week 28) | 46 | | | |
| Number of times to take the medicine (Week 28) | 42 | | | |
| Other (Week 28) | 5 | | | |
| Taste (Week 28) | 30 | | | |
| Aftertaste (Week 48) | 17 | | | |
| Can correctly prepare the medicine (Week 48) | 48 | | | |
| Convenience (Week 48) | 103 | | | |
| Easier to remember to take the medicine (Week 48) | 61 | | | |
| Gain personal time with family/friends (Week 48) | 36 | | | |
| No/ less pain on the injection site (Week 48) | 37 | | | |
| No/ less side effects (Week 48) | 48 | | | |
| Number of pills (Week 48) | 41 | | | |
| Number of times to take the medicine (Week 48) | 47 | | | |
| Other (Week 48) | 0 | | | |
| Taste (Week 48) | 51 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of consumed tablet counts during deferasirox DT and deferasirox FCT treatment periods

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|-----------------|--|
| End point title | Percentage of consumed tablet counts during deferasirox DT |
|-----------------|--|

End point description:

The percentage of consumed tablet counts (compliance) was calculated for each treatment period in the core phase: deferasirox DT (period 1) and deferasirox FCT (period 2). Compliance was defined as the total tablet count consumed divided by total tablet count prescribed and multiplied by 100. Total tablet count consumed was calculated as total number of tablets dispensed minus total number of tablets lost/wasted or returned. Total tablet count prescribed was calculated as the number of tablets that the patient should have taken during this period. If a patient did not return the study drug, the compliance was not calculated.

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|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

| |
|--|
| Deferasirox DT: Baseline Day 1 to Week 24. Deferasirox FCT: Week 25 to Week 48 |
|--|

| End point values | Deferasirox DT followed by deferasirox FCT (Full Analysis Set) | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 139 | | | |
| Units: Percentage of tablet counts | | | | |
| arithmetic mean (standard deviation) | | | | |
| Deferasirox DT (Baseline to Week 24) n=139 | 98.68 (± 22.373) | | | |
| Deferasirox FCT (Week 25 to Week 48) n=138 | 95.07 (± 15.368) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change over time in aftertaste score of palatability questionnaire

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|-----------------|--|
| End point title | Change over time in aftertaste score of palatability questionnaire |
|-----------------|--|

End point description:

The palatability questionnaire consisted of 4 items, three items measuring taste and one item measuring aftertaste. The aftertaste item scored on a 5-point response scale with the response option: Very good = 1, Good = 2, Neither good nor bad = 3, Bad = 4, Very bad = 5. This item offered an additional response option of "no aftertaste". The aftertaste score was calculated among participants who had an aftertaste. Higher aftertaste scores indicated a worse aftertaste.

For participants less than (<) 10 years old, an observer palatability questionnaire was administered. Items and scoring algorithm remained the same as for participants greater than (≥) 10 years old. Change in aftertaste score over time was assessed.

Note: 9999 indicates value is not applicable.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

| |
|-----------------------|
| Week 4, 24, 28 and 48 |
|-----------------------|

| End point values | Deferasirox DT followed by deferasirox FCT (Full Analysis Set) | | | |
|--|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 139 | | | |
| Units: Score on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 - 24: treated with deferasirox DT (n=102) | -0.1 (± 0.80) | | | |
| Week 4 - 24: treated with deferasirox FCT (n=6) | -0.5 (± 1.22) | | | |
| Week 24 - 28: treated with deferasirox DT (n=0) | 9999 (± 9999) | | | |
| Week 24 - 28: treated with deferasirox FCT (n=106) | -0.5 (± 1.16) | | | |
| Week 24 - 48: treated with deferasirox DT (n=0) | 9999 (± 9999) | | | |
| Week 24 - 48: treated with deferasirox FCT (n=98) | -0.5 (± 1.08) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change over time in palatability score of palatability questionnaire

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|-----------------|--|
| End point title | Change over time in palatability score of palatability questionnaire |
|-----------------|--|

End point description:

The palatability questionnaire consisted of 4 items, three items measuring taste and one item measuring aftertaste. Among the taste items, first one measured taste on a 5-point response scale. The palatability questionnaire consisted of 4 items, three items measuring taste and one item measuring aftertaste. Among the taste items, first one measured taste on a 5-point response scale. The other two items measured what happened after taking the medicine and how the perceived amount of liquid taken with the medicine was. Responses to these 3 items were combined and converted into a single palatability score using a scoring matrix: each combination of responses on each of 3 items corresponded to a predefined palatability score. For participants <10 years old, an observer palatability questionnaire was administered. Items and scoring algorithm were the same as for participants ≥10 years old. Change in palatability score over time was assessed.

Note: 9999 indicates value is not applicable

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 4, 24, 28 and 48

| End point values | Deferasirox DT followed by deferasirox FCT (Full Analysis Set) | | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 139 | | | |
| Units: Score on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|--|---------------|--|--|--|
| Week 4 - 24: treated with deferasirox DT (n=131) | -0.1 (± 2.46) | | | |
| Week 4 - 24: treated with deferasirox FCT (n=7) | 0.0 (± 0.00) | | | |
| Week 24 - 28: treated with deferasirox DT (n=0) | 9999 (± 9999) | | | |
| Week 24 - 28: treated with deferasirox FCT (n=137) | 1.1 (± 2.77) | | | |
| Week 24 - 48: treated with deferasirox DT (n=0) | 9999 (± 9999) | | | |
| Week 24 - 48: treated with deferasirox FCT (n=134) | 1.3 (± 2.54) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in adherence domain score of modified satisfaction with iron chelation (mSICT) questionnaire

| | |
|-----------------|---|
| End point title | Change from baseline in adherence domain score of modified satisfaction with iron chelation (mSICT) questionnaire |
|-----------------|---|

End point description:

The mSICT patient reported outcome (PRO) consisted of 15 items that represented 3 domains: Adherence, Preference, and Concerns. The adherence domain score consisted of 6 adherence items, measured using a 5-point response scale. The adherence score was calculated by summing these 6 items, with scores ranging from 6 to 30. Higher scores indicated worse adherence.

For participants <10 years old, an observer version (ObsRO) was administered. The adherence score remained the same as for participants ≥10 years old.

Note: 9999 indicates value is not applicable

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (week 2 or, if missing, week 3), week 24, 28 and 48

| End point values | Deferasirox DT followed by deferasirox FCT (Full Analysis Set) | | | |
|--|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 139 | | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24-treated with deferasirox DT (PRO) (n=72) | -0.3 (± 3.37) | | | |
| Week 24 -treated with deferasirox FCT (PRO) (n=4) | -1.0 (± 2.94) | | | |
| Week 28 -treated with deferasirox DT (PRO) (n=0) | 9999 (± 9999) | | | |
| Week 28 -treated with deferasirox FCT (PRO) (n=77) | 0.5 (± 3.59) | | | |
| Week 48 -treated with deferasirox DT (PRO) (n=0) | 9999 (± 9999) | | | |
| Week 48 -treated with deferasirox FCT (PRO) (n=75) | 0.5 (± 3.29) | | | |

| | | | | |
|---|---------------|--|--|--|
| Week 24-treated with deferasirox DT(ObsRO)(n=56) | -0.2 (± 3.35) | | | |
| Week 24-treated with deferasirox FCT(ObsRO)(n=3) | -0.7 (± 4.16) | | | |
| Week 28-treated with deferasirox DT (ObsRO)(n=0) | 9999 (± 9999) | | | |
| Week 28-treated with deferasirox FCT(ObsRO)(n=58) | 0.8 (± 3.68) | | | |
| Week 48-treated with deferasirox DT(ObsRO)(n=0) | 9999 (± 9999) | | | |
| Week 48-treated with deferasirox FCT(ObsRO)(n=55) | 1.1 (± 3.79) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in preference domain score of modified satisfaction with iron chelation (mSICT) questionnaire

| | |
|-----------------|--|
| End point title | Change from baseline in preference domain score of modified satisfaction with iron chelation (mSICT) questionnaire |
|-----------------|--|

End point description:

The mSICT patient reported outcome (PRO) consisted of 15 items that represented 3 domains: Adherence, Preference, and Concerns.

The preference/satisfaction domain score consisted of 2 preference/satisfaction items, measured using a 5-point response scale. The preference score was calculated by summing these 2 items, with scores ranging from 2 to 10. Higher scores indicated worse satisfaction.

For participants < 10 years old, an observer version (ObsRO) was administered. Preference score remained the same as for participants ≥ 10 years old.

Note: 9999 indicates value is not applicable.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (week 2 or, if missing, week 3), week 24, 28 and 48

| End point values | Deferasirox DT followed by deferasirox FCT (Full Analysis Set) | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 139 | | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24-treated with deferasirox DT(PRO)(n=72) | 0.5 (± 1.21) | | | |
| Week 24-treated with deferasirox FCT(PRO)(n=4) | 0.5 (± 3.70) | | | |
| Week 28-treated with deferasirox DT(PRO)(n=0) | 9999 (± 9999) | | | |
| Week 28-treated with deferasirox FCT(PRO)(n=77) | -1.1 (± 1.83) | | | |
| Week 48-treated with deferasirox DT(PRO)(n=0) | 9999 (± 9999) | | | |

| | | | | |
|---|---------------|--|--|--|
| Week 48-treated with deferasirox FCT(PRO)(n=75) | -0.9 (± 2.02) | | | |
| Week 24-treated with deferasirox DT(ObsRO)(n=55) | 0.0 (± 1.49) | | | |
| Week 24-treated with deferasirox FCT(ObsRO)(n=3) | 0.0 (± 1.73) | | | |
| Week 28-treated with deferasirox DT(ObsRO)(n=0) | 9999 (± 9999) | | | |
| Week 28-treated with deferasirox FCT(ObsRO)(n=57) | -0.8 (± 1.74) | | | |
| Week 48-treated with deferasirox DT(ObsRO)(n=0) | 9999 (± 9999) | | | |
| Week 48-treated with deferasirox FCT(ObsRO)(n=54) | -0.9 (± 1.75) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in concerns domain score of modified satisfaction with iron chelation (mSICT) questionnaire

| | |
|-----------------|--|
| End point title | Change from baseline in concerns domain score of modified satisfaction with iron chelation (mSICT) questionnaire |
|-----------------|--|

End point description:

The mSICT patient reported outcome (PRO) consisted of 15 items that represented 3 domains: Adherence, Preference, and Concerns.

The concerns domain score consisted of 3 items to address any concerns or worries with the medication. All 3 items were measured on a 5-point response scale. The concerns score was calculated by summing the 3 items, with scores ranging from 3 to 15. Higher scores indicated fewer concerns. For participants < 10 years old, an observer version (ObsRO) was administered. Concerns score remained the same as for participants ≥ 10 years old.

Note: 9999 indicates value is not applicable

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (week 2 or, if missing, week 3), week 24, 28 and 48

| End point values | Deferasirox DT followed by deferasirox FCT (Full Analysis Set) | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 139 | | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24-treated with deferasirox DT(PRO)(n=72) | -0.1 (± 1.99) | | | |
| Week 24-treated with deferasirox FCT(PRO)(n=4) | -1.0 (± 1.15) | | | |
| Week 24-treated with deferasirox DT (PRO)(n=0) | 9999 (± 9999) | | | |
| Week 28-treated with deferasirox FCT(PRO)(n=77) | 0.3 (± 1.84) | | | |

| | | | | |
|---|---------------|--|--|--|
| Week 48-treated with deferasirox DT (PRO)(n=0) | 9999 (± 9999) | | | |
| Week 48-treated with deferasirox FCT(PRO)(n=75) | 0.5 (± 1.80) | | | |
| Week 24-treated with deferasirox DT (ObsRO)(n=55) | -0.4 (± 1.33) | | | |
| Week 24-treated with deferasirox FCT(ObsRO)(n=3) | -0.7 (± 1.15) | | | |
| Week 28-treated with deferasirox DT (ObsRO)(n=0) | 9999 (± 9999) | | | |
| Week 28-treated with deferasirox FCT(ObsRO)(n=58) | 0.1 (± 2.05) | | | |
| Week 48-treated with deferasirox DT(ObsRO)(n=0) | 9999 (± 9999) | | | |
| Week 48-treated with deferasirox FCT(ObsRO)(n=54) | 0.1 (± 1.58) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in gastrointestinal (GI) symptom score based on GI questionnaire

| | |
|-----------------|---|
| End point title | Change from baseline in gastrointestinal (GI) symptom score based on GI questionnaire |
|-----------------|---|

End point description:

The GI symptom score was calculated from responses to 5 questions of the GI questionnaire, each with a possible score of 1 to 5, for an overall possible score range of 5 to 25, where a lower score represents a less severe GI symptom and a higher score represents a more severe GI symptom.

An observer GI symptom questionnaire was administered to those patients who were < 10 years old.

The questionnaire was completed by the parents of the participants. All items and the scoring algorithm remained the same as for participants ≥ 10 years old.

Note: 9999 indicates value is not applicable

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (week -1 or, if missing, week -2), week 24, 28 and 48

| | | | | |
|---|--|--|--|--|
| End point values | Deferasirox DT followed by deferasirox FCT (Full Analysis Set) | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 139 | | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 <10yrs treated with deferasirox DT(n=60) | 0.2 (± 2.78) | | | |
| Week 24 <10yrs treated with deferasirox FCT(n=3) | -2.0 (± 2.65) | | | |
| Week 28 <10yrs treated with deferasirox DT(n=0) | 9999 (± 9999) | | | |
| Week 28 <10yrs treated with deferasirox FCT(n=62) | -0.5 (± 2.49) | | | |

| | | | | |
|---|---------------|--|--|--|
| Week 48 <10yrs treated with deferasirox DT(n=0) | 9999 (± 9999) | | | |
| Week 48 <10yrs treated with deferasirox FCT(n=61) | -0.6 (± 2.33) | | | |
| Week 24 ≥10yrs treated with deferasirox DT(n=71) | 1.4 (± 5.53) | | | |
| Week 24 ≥10yrs treated with deferasirox FCT(n=4) | 5.8 (± 12.82) | | | |
| Week 28 ≥10yrs treated with deferasirox DT(n=0) | 9999 (± 9999) | | | |
| Week 28 ≥10yrs treated with deferasirox FCT(n=75) | -1.9 (± 4.33) | | | |
| Week 48 ≥10yrs treated with deferasirox DT(n=0) | 9999 (± 9999) | | | |
| Week 48 ≥10yrs treated with deferasirox FCT(n=75) | -2.2 (± 4.74) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in serum ferritin levels

| | |
|--|---|
| End point title | Change from baseline in serum ferritin levels |
| End point description: | |
| Absolute change from baseline over time in serum ferritin levels | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 1) up to 96 weeks | |

| End point values | Deferasirox DT followed by deferasirox FCT (Full Analysis Set) | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 139 | | | |
| Units: microgram/liter (ug/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 2 - treated with deferasirox DT(n=108) | 363.654 (± 323.3828) | | | |
| Week 4 - treated with deferasirox DT (n=120) | 393.126 (± 457.8032) | | | |
| Week 8 - treated with deferasirox DT (n=121) | 462.560 (± 427.7138) | | | |
| Week 12 - treated with deferasirox DT (n=129) | 510.455 (± 548.6222) | | | |
| Week 16 - treated with deferasirox DT (n=131) | 519.038 (± 508.7432) | | | |
| Week 20 - treated with deferasirox DT (n=134) | 540.618 (± 548.2318) | | | |
| Week 24 - treated with deferasirox DT (n=130) | 644.849 (± 629.6687) | | | |

| | | | | |
|--|------------------------|--|--|--|
| Week 28 - treated with deferasirox FCT (n=114) | 679.610 (± 701.6219) | | | |
| Week 32 - treated with deferasirox FCT (n=126) | 623.600 (± 629.5417) | | | |
| Week 36 - treated with deferasirox FCT (n=127) | 679.011 (± 674.6716) | | | |
| Week 40 - treated with deferasirox FCT (n=120) | 739.016 (± 659.0840) | | | |
| Week 44 - treated with deferasirox FCT (n=120) | 748.063 (± 647.3000) | | | |
| Week 48 - treated with deferasirox FCT (n=120) | 833.700 (± 788.0650) | | | |
| Week 52 - treated with deferasirox FCT | 760.229 (± 798.0836) | | | |
| Week 56 - treated with deferasirox FCT (n=113) | 903.622 (± 832.9872) | | | |
| Week 60 - treated with deferasirox FCT (n=106) | 980.644 (± 994.4445) | | | |
| Week 64 - treated with deferasirox FCT (n=102) | 863.579 (± 854.8592) | | | |
| Week 68 - treated with deferasirox FCT (n=92) | 921.725 (± 860.8738) | | | |
| Week 72 - treated with deferasirox FCT (n=91) | 971.112 (± 872.7306) | | | |
| Week 76 - treated with deferasirox FCT (n=90) | 888.917 (± 869.0805) | | | |
| Week 80 - treated with deferasirox FCT (n=77) | 1005.758 (± 868.4338) | | | |
| Week 84 - treated with deferasirox FCT (n=87) | 1013.683 (± 924.5828) | | | |
| Week 88 - treated with deferasirox FCT (n=80) | 1117.849 (± 985.0767) | | | |
| Week 92 - treated with deferasirox FCT (n=74) | 1222.429 (± 1027.2565) | | | |
| Week 96 - treated with deferasirox FCT (n=74) | 1137.347 (± 972.1286) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from day of first dose to 30 days after last dose of study medication, assessed up to approx. 30 weeks for deferasirox DT treatment, 39 weeks for deferasirox FCT treatment and 70 weeks for deferasirox FCT treatment

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | Deferasirox DT (Core Phase) |
|-----------------------|-----------------------------|

Reporting group description:

Participants who were treated with deferasirox DT once daily in the core phase

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Deferasirox FCT (Extension phase) |
|-----------------------|-----------------------------------|

Reporting group description:

Participants who were treated with deferasirox FCT once daily in the extension phase

| | |
|-----------------------|------------------------------|
| Reporting group title | Deferasirox FCT (Core Phase) |
|-----------------------|------------------------------|

Reporting group description:

Participants who were treated with deferasirox FCT once daily in the core phase

| Serious adverse events | Deferasirox DT (Core Phase) | Deferasirox FCT (Extension phase) | Deferasirox FCT (Core Phase) |
|---|-----------------------------|-----------------------------------|------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 148 (8.78%) | 16 / 116 (13.79%) | 6 / 140 (4.29%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cholangiocarcinoma | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 148 (0.68%) | 0 / 116 (0.00%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 148 (0.68%) | 2 / 116 (1.72%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 148 (1.35%) | 1 / 116 (0.86%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 3 / 3 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 148 (1.35%) | 0 / 116 (0.00%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 148 (0.68%) | 0 / 116 (0.00%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 1 / 148 (0.68%) | 0 / 116 (0.00%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Abdominal injury | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal injury | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Splenic rupture | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ulna fracture | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 1 / 148 (0.68%) | 0 / 116 (0.00%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 116 (0.00%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Polyneuropathy | | | |
| subjects affected / exposed | 1 / 148 (0.68%) | 0 / 116 (0.00%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Haemolysis | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Leukopenia | | | |
| subjects affected / exposed | 2 / 148 (1.35%) | 0 / 116 (0.00%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 148 (1.35%) | 0 / 116 (0.00%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Optic nerve cupping | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholangitis acute | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 148 (0.68%) | 0 / 116 (0.00%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 148 (0.68%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 148 (0.68%) | 1 / 116 (0.86%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 0 / 116 (0.00%) | 1 / 140 (0.71%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 148 (0.68%) | 0 / 116 (0.00%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ecthyma | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 148 (0.68%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 148 (0.00%) | 1 / 116 (0.86%) | 0 / 140 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Deferasirox DT (Core Phase) | Deferasirox FCT (Extension phase) | Deferasirox FCT (Core Phase) |
|---|--------------------------------|--------------------------------------|---------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 82 / 148 (55.41%) | 49 / 116 (42.24%) | 59 / 140 (42.14%) |
| Investigations | | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 5 / 148 (3.38%) | 6 / 116 (5.17%) | 4 / 140 (2.86%) |
| occurrences (all) | 7 | 6 | 6 |

| | | | |
|---|-------------------------|-------------------------|------------------------|
| Serum ferritin increased subjects affected / exposed occurrences (all) | 8 / 148 (5.41%) 9 | 1 / 116 (0.86%) 1 | 2 / 140 (1.43%) 2 |
| Urine protein/creatinine ratio increased subjects affected / exposed occurrences (all) | 13 / 148 (8.78%) 15 | 7 / 116 (6.03%) 8 | 12 / 140 (8.57%) 14 |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 7 / 148 (4.73%) 7 | 5 / 116 (4.31%) 10 | 8 / 140 (5.71%) 8 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 16 / 148 (10.81%) 17 | 2 / 116 (1.72%) 3 | 5 / 140 (3.57%) 5 |
| Hepatobiliary disorders Hepatomegaly subjects affected / exposed occurrences (all) | 8 / 148 (5.41%) 8 | 0 / 116 (0.00%) 0 | 0 / 140 (0.00%) 0 |
| Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all) | 8 / 148 (5.41%) 8 | 12 / 116 (10.34%) 18 | 9 / 140 (6.43%) 10 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 6 / 148 (4.05%) 6 | 3 / 116 (2.59%) 3 | 7 / 140 (5.00%) 9 |
| Pharyngitis subjects affected / exposed occurrences (all) | 7 / 148 (4.73%) 10 | 6 / 116 (5.17%) 7 | 6 / 140 (4.29%) 7 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 8 / 148 (5.41%) 9 | 4 / 116 (3.45%) 4 | 8 / 140 (5.71%) 8 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 9 / 148 (6.08%) 9 | 3 / 116 (2.59%) 3 | 3 / 140 (2.14%) 3 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 12 February 2019 | The purpose of this amendment was to provide additional clarity to the study Investigators in relation to dosing of deferasirox for patients with non-transfusion dependent thalassemia (NTDT), those patients changing therapy from deferiprone, and those patients with body weight lower than 20 kg; to provide additional guidance in relation to the ocular and auditory assessments; to revise the underlying assumptions used to calculate the sample size of the study; to clarify the inclusion criterion that relates to prior therapy; to correct inconsistencies and typos; and to update withdrawal of consent language. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, no statistical analyses have been specified for the endpoints, as this is a single arm study and comparisons within an arm are not supported by the system. Please use <https://www.novctrd.com/> for complete results.

Notes: